CLAIMS

We claim:

[0168] 1. A method comprising the steps of:

positioning a probe adjacent a tissue site of an animal including a human;

injecting a contrast agent into the animal at an injection site;

acquiring data before and after injection;

performing a difference analysis between pre-injection data and post-injection data to detect, localize, and quantify anatomical, morphological and/or functional features of the tissue site.

[0169] 2. A method comprising the steps of:

positioning a probe adjacent a tissue site of an animal including a human;

acquiring a pre-injection data of the tissue site;

injecting a contrast agent into the animal at an injection site;

acquiring a post-injection data of the tissue site;

performing a difference analysis between the pre-injection data and post-injection data to detect, localize, and quantify anatomical, morphological and/or functional features of the tissue site over a total data acquisition time.

[0170] 3. A method comprising the steps of:

positioning a probe adjacent a tissue site of an animal including a human;

acquiring a pre-injection data sequence of the tissue site over a pre-injection period of time;

positioning a contrast agent delivery system in an artery supply blood to the tissue site or in a vein removing blood from the tissue site;

injecting a contrast agent into the artery or the vein;

acquiring a post-injection data sequence of the tissue site over a post-injection period of time; and

performing a difference analysis between the pre-injection data and post-injection data to detect, localize, and quantify anatomical, morphological and/or functional features of the tissue site over a total data acquisition time.

[0171] 4. A method comprising the steps of:

positioning a guide-catheter in a vessel;

positioning a micro-catheter including a probe in the vessel at a site to be imaged;

acquiring a pre-injection data sequence for a pre-injection period of time;

injecting a contrast agent into the vessel over an injection period from a contrast agent delivery system;

continuing to acquire IVUS images to form a during-injection, IVUS image sequence over a during injection period of time;

injecting normal saline to flush contrast agent from the delivery system;

continuing to acquire IVUS images to form a post-injection, IVUS image sequence over a post-injection period of time;

performing an automated difference analysis between the pre-injection image sequence and the post-injection image sequence to detect, localize, and quantify structural features of the site over a total data acquisition time.

[0172] 5. The method of any one of the preceding claims, further comprising the step of:

forming pre phase-correlated data from the pre-injection data and post phase-correlated data from the post-injection data.

[0173] 6. The method of claim 5, further comprising the step of:

selecting a region of interest within the pre and post phase-correlated data.

[0174] 7. The method of claim 6, further comprising the step of:

compensating for relative motion of the region of interest in the pre an post phase-correlated data.

[0175] 8. The method of claim 7, further comprising the step of:

filtering the motion compensating pre and post phase-correlated data.

[0176] 9. The method of claim 8, further comprising the step of:

reconstruction the filtered, motion compensated pre and post phase-correlated data.

[0177] 10. The method of claim 9, further comprising the step of:

identifying enhancements in the region of interest as a function of a data acquisition time:

[0178] 11. The method of claims 2, 3, or 4, wherein the data acquisition time is from about 0.5 minutes to about 30 minutes.

[0179] 12. The method of claims 2, 3, or 4, further comprising the step of:

acquiring a during-injection data sequence of the tissue site.

[0180] 13. The method of claim 2, 3, or 4, wherein the pre-injection data is acquired over a pre-injection period of time ranging from about 1 second to about 10 minutes.

[0181] 14. The method of claim 2, 3, or 4, wherein the post-injection data is acquired over a post-injection period of time ranging from about 1 second to about 20 minutes.

[0182] 15. The method of claim 12, wherein the during-injection data is acquired over a during-injection period of time comprising a duration of the contrast agent injection.

[0183] 16. The method of any one of the preceding claims, wherein the data or data sequences are digitized and automatically sorted and binned according to their temporal position in each of a sequence of cardiac phases over the total acquisition time.

[0184] 17. The method of any one of the preceding claims, further comprising the step of:

generating difference data or image sequences between data or frames in the pre- and post-injection data or data sequences.

[0185] 18. The method of any one of the preceding claims, further comprising the step of:

performing noise reduction on the data or IVUS frames prior to difference analysis via mathematical averaging of temporally correlated data or frames, where temporal correlated data

or images are data or images binned at a same point in a cardiac cycle.

[0186] 19. The method of any one of the preceding claims, further comprising the step of:

automatically thresholding the difference data or images to separate regions of salient grey-level enhancements.

[0187] 20. The method of claims 19, further comprising the step of:

color-coding the thresholded difference data or images to indicate a location and strength of the enhancements.

[0188] 21. The method of any one of the preceding claims, further comprising the step of:

generating an animation of changes in enhancements over the total acquisition time of the difference data or images, thresholded data or images and/or the color-coded data or images.

[0189] 22. The method as set forth in claim 21, wherein the animation resulting from this method has a frame-to-frame correspondence with the originally-acquired IVUS sequence in order to allow direct visual comparison between the original data and the processed data.

[0190] 23. The method of any one of the preceding claims, further comprising:

computing a statistical measurement of an average enhancement per enhanced pixel for each difference data or image generated over the total acquisition time to quantify numerically a presence and amount of enhancements over time.

[0191] 24. The method of claims 23, wherein the enhancements are evidence of vasa vasorum or other structures associated with the site.

[0192] 25. The method of claim 24, wherein the other structures include plaque, calcified plaque, malignancy structure, malignancy vascularization.

[0193] 26. The method of any one of the preceding claims, wherein the probe is selected from the group consisting of an ultrasound probe, a variable frequency ultrasound probe, a

magnetic probe, a photonic probe, a near Infrared probe, a terrahertz probe, microwave probe and combinations thereof.

[0194] 27. The method of any one of the preceding claims, wherein the contrast agent is selected from the group consisting of microbubbles, magnetically active microbubbles, magnetically active nanoparticles, near Infrared visible microbubbles, near Infrared visible nanoparticles, optically visible microbubbles, optically visible nanoparticles, terrahertz visible microbubbles, terrahertz visible nanoparticles, microwave visible microbubbles, microwave visible nanoparticles, red blood or stem cells including magnetically active nanoparticles, near Infrared visible nanoparticles, optically visible nanoparticles, terrahertz visible nanoparticles, microwave visible nanoparticles, and mixtures thereof, and mixtures or combinations thereof.

[0195] 28. The method of any one of the preceding claims, further comprising the steps of:

positioning a balloon in an artery supplying blood to or a vein removing blood from the site; and

inflating or partially inflating the balloon to alter a blood flow into the site during data acquisition;

deflating the balloon during data acquisition.

[0196] 29. The method of claim 28, wherein the inflating and deflating steps are performed periodically at a given periodicity.

[0197] 30. The method of any one of the preceding claims, further comprising the step of:

exposing the site, after contract agent injection, to a sonic energy at a frequency sufficient to cause a position of each contrast agent to periodically change.

[0198] 31. The method of any one of the preceding claims, further comprising the step of:

exposing the site, after contract agent injection, to a sonic energy at a frequency sufficient to destroy the contrast agent.

[0199] 32. A catheter apparatus comprising:

a guide-catheter adapted to be inserted into a peripheral vessel and then positioned in a target vessel; and

a contrast agent delivery system designed to inject an amount of contrast agent into the vessel.

[0200] 33. The apparatus of claim 32, further comprising:

at least one guide-wire adapted to be extended from a distal end of the guide-catheter into the vessel; and

at least one micro-catheter having an central orifice and adapted to slide down the guide wire to a desired location in the vessel.

[0201] 34. The apparatus of claims 32 or 33, further comprising:

a balloon adapted to augment a flow of blood in the vessel.

[0202] 35. The apparatus of claims 32 or 33, wherein the micro-catheter includes a probe.

[0203] 36. The apparatus of claims 32 or 33, wherein the micro-catheter includes a plurality of probes.

[0204] 37. The apparatus of claims 32, 33, 34, 35 or 36, wherein the contrast agent delivery system forms a part of the micro-catheter.

[0205] 38. The apparatus of claim 37, wherein the contrast agent delivery system is upstream of the probe or probes.

[0206] 39. The apparatus of claims 34, 35, 36, 37 or 38, wherein the balloon is upstream of the probe or probes.

[0207] 40. The apparatus of claims 28, 29, 30, 31, 32 or 33, wherein the probe is selected from the group consisting of an ultrasound probe, a variable frequency ultrasound probe, a magnetic probe, a photonic probe, a near Infrared probe, a terrahertz probe, microwave probe and

combinations thereof.

[0208] 41. The apparatus of claims 28, 29, 30, 31, 32 or 33, wherein the contrast agent is selected from the group consisting of microbubbles, magnetically active microbubbles, magnetically active nanoparticles, near Infrared visible microbubbles, near Infrared visible nanoparticles, optically visible microbubbles, optically visible nanoparticles, terrahertz visible microbubbles, terrahertz visible nanoparticles, microwave visible microbubbles, microwave visible nanoparticles, red blood or stem cells including magnetically active nanoparticles, near Infrared visible nanoparticles, optically visible nanoparticles, terrahertz visible nanoparticles, microwave visible nanoparticles, and mixtures thereof, and mixtures or combinations thereof.